

IN THE CLAIMS

1. (Original) An automated method for the large-scale *in vitro* screening of cells secreting at least one specific monoclonal antibody with affinity for a compound of interest, said method comprising at least the following steps:

(10) distribution of antibody-producing cells in at least one well of at least one culture plate;

(12) culturing said cells under conditions allowing their growth, with concomitant detection of cellular growth and of the quality of the cultures;

(14) iterative screening of said cells for the secretion of antibodies, with cloning of the cells secreting at least one antibody interacting with said compound of interest; and

(16) selection of at least one cell secreting one specific monoclonal antibody with affinity for said compound of interest.

2. (Currently Amended) The method as claimed in claim 1, ~~characterized in that~~ wherein said compound of interest is an antigen comprising at least one epitope.

3. (Currently Amended) The method as claimed in claim 2, ~~characterized in that~~ wherein said antigen is chosen from the group consisting of proteins, nucleic acids, viral particles, synthetic peptides, chemical compounds, organs, organelles, whole cells, and subcellular fragmentations.

4. (Currently Amended) The method as claimed in claim 3, ~~characterized in that~~ wherein said antigen is a tumor cell.

5. (Currently Amended) The method as claimed in claim 1, ~~characterized in that~~ wherein said distribution according to step (10) is carried out in an amount of at least 3×10^5 cells per well.

6. (Currently Amended) The method as claimed in claim 1, ~~characterized in that~~ wherein each step is performed in a sterile atmosphere.

7. (Currently Amended) The method as claimed in claim 1, ~~characterized in that~~ wherein said step (10) is at least preceded by the following preliminary steps:

- (1) immunization of at least one animal, with said compound of interest;
- (2) optionally, measurement of the immune response of said animal; and
- (3) recovery of the antibody-producing cells.

8. (Currently Amended) The method as claimed in claim 1, ~~characterized in that~~ wherein said step (10) is at least preceded by the following preliminary steps:

- (0) bringing at least one dendritic cell and said compound of interest into contact, such that said dendritic cell presents at least one epitope of said compound of interest;
- (1) immunization of at least one animal, with said dendritic cell presenting said epitope;
- (2) optionally, measurement of the immune response of said animal; and
- (3) recovery of the antibody-producing cells.

9. (Currently Amended) The method as claimed in claim 8, ~~characterized in that~~ wherein, when said compound of interest is a tumor cell, said step (0) comprises at least:

- (01) the fusion of said dendritic cell and said tumor cell; and
- (02) the recovery of at least one hybrid dendritic cell.

10. (Currently Amended) The method as claimed in claim 7, ~~or 8,~~
~~characterized in that~~ wherein said preliminary steps
additionally comprise:

- (4) the fusion of said antibody-producing cells with
immortalized cells; and
- (5) the recovery of the immortalized antibody-producing cells.

11. (Currently Amended) The method as claimed in claim 7, ~~or 8,~~
~~characterized in that~~ wherein said antibody-producing cells are
chosen from the group consisting of mouse, rat, rabbit, and ~~or~~
human cells.

12. (Currently Amended) The method as claimed in claim 11,
~~characterized in that~~ wherein said antibody-producing cells are
mouse cells.

13. (Currently Amended) The method as claimed in ~~any one of~~
~~claims 7, to 12, characterized in that~~ wherein said preliminary
steps are not automated.

14. (Currently Amended) The method as claimed in claim 1,
~~characterized in that~~ wherein said iterative screening step (14)
comprises at least the following screening module, which may be
repeated:

- transfer of the culture medium collected from at least
one well of at least one culture plate, into at least one well
of at least one screening plate;
- screening of the cells for at least one given selection
criterion;
- selective subculturing of the cells satisfying said
criterion into at least one well of at least one new culture
plate; and

- culture of said cells under conditions allowing their growth, with concomitant detection of cell growth and of the quality of the cultures.

15. (Currently Amended) The method as claimed in claim 14, ~~characterized in that~~ wherein said step (14) comprises a prescreening module in which said selection criterion is the secretion of antibodies:

- (140) transfer of the culture medium to at least one well of at least one screening plate;
- (141) prescreening of the cells for the secretion of antibodies;
- (142) selective subculturing of the cells secreting at least one antibody on at least one culture plate; and
- (143) culture of said cells.

16. (Currently Amended) The method as claimed in claim 14, ~~characterized in that~~ wherein said step (14) comprises a primary screening module in which said selection criterion is the secretion of antibodies interacting with said compound of interest:

- (144) transfer of the culture medium to at least one well of at least one screening plate;
- (145) primary screening of said cells for the secretion of at least one antibody interacting with said compound of interest;
- (146) cloning of the cells secreting at least one antibody interacting with said compound of interest;
- (147) subculturing of the cloned cells on at least one culture plate; and
- (148) culture of said cells.

17. (Canceled)

18. (Currently Amended) The method as claimed in claim 16, ~~or 17, characterized in that~~ wherein said step (14) additionally comprises a secondary screening module, in which said selection criterion is the secretion of monoclonal antibodies specific for said compound of interest:

(149) transfer of the culture medium to at least one well of at least one screening plate;

(150) secondary screening of said cells for the secretion of a monoclonal antibody specific for said compound of interest;

(151) selective subculturing of the cells secreting a monoclonal antibody specific for said compound of interest on at least one culture plate; and

(152) culture of said cells.

19. (Currently Amended) The method as claimed in claim 18, ~~characterized in that~~ wherein said step (14) additionally comprises a tertiary screening module, in which said selection criterion is the secretion of specific monoclonal antibodies with affinity for said compound of interest:

(153) transfer of the culture medium to at least one well of at least one screening plate;

(154) tertiary screening of said cells for the secretion of a specific monoclonal antibody with affinity for said compound of interest; and

(155) optionally, selective subculturing of the cells secreting a specific monoclonal antibody with affinity for said compound of interest on at least one culture plate; and

(156) optionally, culture of said cells.

20. (Currently Amended) The method as claimed in claim 1, ~~characterized in that~~ wherein said step (16) comprises:

(16) the selection of at least one cell secreting a monoclonal antibody with specificity and/or affinity for said compound of

interest greater than those of the monoclonal antibodies secreted by the other cells.

21. (Currently Amended) The method as claimed in claim 1, ~~or 14, characterized in that~~ wherein said culture is carried out over a period of between at least 7 days and at most 21 days, ~~said period being preferably between 7 and 15 days.~~

22. (Currently Amended) The method as claimed in claim 14, ~~characterized in that~~ wherein a cell library is prepared for at least one screening module.

23. (Currently Amended) The method as claimed in claim 15, ~~characterized in that~~ wherein said step (141) comprises at least:

- (1411) the detection of the secretion of antibodies; and
- (1412) the selection of cells secreting at least one antibody.

24. (Currently Amended) The method as claimed in claim 23, ~~characterized in that~~ wherein said step (1411) comprises at least:

- (14111) the collection of at least one culture supernatant sample; and
- (14112) the detection of the secretion of antibodies in said sample.

25. (Currently Amended) The method as claimed in claim 23, ~~characterized in that~~ wherein said step (1411) comprises at least the detection of the secretion of antibodies directly in the wells.

26. (Currently Amended) The method as claimed in claim 16, ~~characterized in that~~ wherein said step (145) comprises at least:

(1451) the collection of at least one culture supernatant sample;

(1452) the detection, in said sample, of the interaction of the antibodies with said compound of interest; and

(1453) the selection of cells secreting at least one antibody interacting with said compound of interest.

27. (Currently Amended) The method as claimed in claim 18, ~~characterized in that~~ wherein said step (150) comprises at least:

(1501) the collection of at least one culture supernatant sample;

(1502) the detection, in said sample, of a specific interaction between a monoclonal antibody and said compound of interest; and

(1503) the selection of cells secreting a monoclonal antibody specific for said compound of interest.

28. (Currently Amended) The method as claimed in claim 19, ~~characterized in that~~ wherein said step (154) comprises at least:

(1541) the collection of at least one culture supernatant sample; and

(1542) the measurement of the affinity of a monoclonal antibody for said compound of interest.

29. (Currently Amended) The method as claimed in claim 28, ~~characterized in that~~ wherein step (1542) comprises at least:

(15421) the measurement of the affinity of a monoclonal antibody for said compound of interest; and

(15422) the identification and/or the location of at least one epitope of said compound of interest.

30. (Currently Amended) The method as claimed in claim 29, ~~characterized in that~~ wherein said steps (15421) and (15422) are concomitant.

31. (Currently Amended) The method as claimed in claim 28, ~~characterized in that~~ wherein step (154) additionally comprises: (1543) the classification of the monoclonal antibodies on the basis of their specificity and/or their affinity for said compound of interest.

32. (New) The method as claimed in claim 8, wherein said preliminary steps additionally comprise:

(4) the fusion of said antibody-producing cells with immortalized cells; and

(5) the recovery of the immortalized antibody-producing cells.

33. (New) The method as claimed in claim 8, wherein said antibody-producing cells are chosen from the group consisting of mouse, rat, rabbit, and human cells.

34. (New) The method as claimed in claim 33, wherein said antibody-producing cells are mouse cells.

35. (New) The method as claimed in claim 8, wherein said preliminary steps are not automated.

36. (New) The method as claimed in claim 10, wherein said preliminary steps are not automated.

37. (New) The method as claimed in claim 32, wherein said preliminary steps are not automated.

38. (New) The method as claimed in claim 14, wherein said step (14) comprises:

(a) a prescreening module in which said selection criterion is the secretion of antibodies:

(140) transfer of the culture medium to at least one well of at least one screening plate;

(141) prescreening of the cells for the secretion of antibodies;

(142) selective subculturing of the cells secreting at least one antibody on at least one culture plate; and

(143) culture of said cells; and

(b) a primary screening module in which said selection criterion is the secretion of antibodies interacting with said compound of interest:

(144) transfer of the culture medium to at least one well of at least one screening plate;

(145) primary screening of said cells for the secretion of at least one antibody interacting with said compound of interest;

(146) cloning of the cells secreting at least one antibody interacting with said compound of interest;

(147) subculturing of the cloned cells on at least one culture plate; and

(148) culture of said cells.

39. (New) The method as claimed in claim 38, wherein said step (14) additionally comprises a secondary screening module, in which said selection criterion is the secretion of monoclonal antibodies specific for said compound of interest:

(149) transfer of the culture medium to at least one well of at least one screening plate;

(150) secondary screening of said cells for the secretion of a monoclonal antibody specific for said compound of interest;

(151) selective subculturing of the cells secreting a monoclonal antibody specific for said compound of interest on at least one culture plate; and

(152) culture of said cells.

40. (New) The method as claimed in claim 39, wherein said step (14) additionally comprises a tertiary screening module, in which said selection criterion is the secretion of specific monoclonal antibodies with affinity for said compound of interest:

(153) transfer of the culture medium to at least one well of at least one screening plate;

(154) tertiary screening of said cells for the secretion of a specific monoclonal antibody with affinity for said compound of interest; and

(155) optionally, selective subculturing of the cells secreting a specific monoclonal antibody with affinity for said compound of interest on at least one culture plate; and

(156) optionally, culture of said cells.

41. (New) The method as claimed in claim 14, wherein said culture is carried out over a period of between at least 7 days and at most 21 days.

42. (New) The method as claimed in claim 21, wherein said period is between 7 and 15 days.

43. (New) The method as claimed in claim 41, wherein said period is between 7 and 15 days.

44. (New) The method as claimed in claim 39, wherein said step (150) comprises at least:

(1501) the collection of at least one culture supernatant sample;

(1502) the detection, in said sample, of a specific interaction between a monoclonal antibody and said compound of interest; and

(1503) the selection of cells secreting a monoclonal antibody specific for said compound of interest.

45. (New) The method as claimed in claim 40, wherein said step (154) comprises at least:

(1541) the collection of at least one culture supernatant sample; and

(1542) the measurement of the affinity of a monoclonal antibody for said compound of interest.

46. (New) The method as claimed in claim 45, wherein step (1542) comprises at least:

(15421) the measurement of the affinity of a monoclonal antibody for said compound of interest; and

(15422) the identification and/or the location of at least one epitope of said compound of interest.

47. (New) The method as claimed in claim 46, wherein said steps (15421) and (15422) are concomitant.

48. (New) The method as claimed in claim 45, wherein step (154) additionally comprises:

(1543) the classification of the monoclonal antibodies on the basis of their specificity and/or their affinity for said compound of interest.